REMARKS

Claims 31, 45-48 are amended. Claims 42-44 are cancelled. Claims 49-68 are added. Claims 31-41 and 45-68 are pending.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Rejection of Claims 42-48 under 35 U.S.C. 112

Claims 42-48 are rejected under 35 U.S.C. 112 as allegedly lacking enablement. The Examiner states that although the claims are enabled for a variant of SEQ ID NO:2, they lack enablement for a variant having between 70-99% identity to SEQ ID NO:2. According to the rejection, the specification fails to enable an artisan to make the claimed mutations in ***any*** alpha-amylase other than one specific sequence, SEQ ID NO:2.

This rejection is respectfully traversed. As amended, the claims recite that the variant has at least 90% identity to SEQ ID NO:2. Claims 45-48 have also been amended to clarify that the the variant has the recited identity, rather than that the parent has the recited identity. This amendment further increases the structural relatedness that the variants has to the fungal alpha-amylase of SEQ ID NO:2.

It is respectfully submitted that an artisan is enabled to practice the invention by preparing variants having the claimed alterations in highly homologous alpha-amylase having at least 90% identity to SEQ ID NO:2 with a reasonable expectation of success. The specification discloses many other alterations that could be made to SEQ ID NO:2, in addition to the claimed alterations. In fact, Applicants have a prior U.S. patent, US Pat. No. 7,005,288, the parent application to this case, which claims many of these other disclosed alterations. The Examiner's conclusion that an artisan is not enabled to make even these additional alterations is clearly inconsistent with this prior determination of the USPTO.

The Examiner's conclusion also does not give appropriate consideration to the very high level of skill in the art. For example, an artisan, at the time of the invention, was routinely able to produce alpha-amylases having the claimed alterations and having at least 90% identity to SEQ ID NO:2, such as, by site directed mutagenesis or random mutagenesis. These tasks are not an "undue burden" on the artisan, but are routine tasks well within the skills of an artisan. Given the very high level of skill in the art, once apprised of Applicants' invention, it is simply routine practice for an artisan to make polypeptides that are at least 90% identical to SEQ ID NO:2 and have the

claimed alterations, using, for example, well-known molecular biological techniques used for obtaining highly homologous polypeptides. Indeed, one skilled in the art would have a very high degree of predictability of being able to make such polypeptides. Furthermore, to the extent that an artisan would encounter sequences which do not have alpha-amylase activity, such sequences are excluded from the claims as the claims require that "the variant has alpha-amylase activity."

The Examiner alleges that the specification fails to provide any guidance for how to identify corresponding positions in other amino acid sequences. However, this is also a skill that is unquestionably routine in the art, and is very easy to perform for enzymes which have a high degree of sequence identity to the reference sequence. In fact, an artisan simply needs to align the sequences to find which amino acids correspond to the recited positions using well known computer programs (e.g., the GAP program using the Needleman and Wunsh algorithm recited in the specification on page 10) or even by eye. It is noted that the Examiner did not have any difficulty finding "corresponding" amino acids in the very low homologous bacterial alpha-amylase of Svendsen et al., yet the Examiner now alleges that an artisan cannot carryout this task for even more highly related sequences. This conclusion cannot be correct and is contrary to the standard practices in the art.

Furthermore, the rejection appears to be based on an erroneous application of the legal standard, namely, that enablement is precluded by the necessity of some experimentation. The test for determining enablement is not whether any experimentation is required, but rather whether undue experimentation is required. As noted by the *In re Wands* court (*In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), the test for determining whether undue experimentation is required even permits a considerable amount of testing. The experimentation that would be required by the present invention is clearly not undue, but rather involves only routine testing, such as to produce/screen for alpha-amylases which are highly homologous to SEQ ID NO:2. Accordingly, even though the experimentation involved might be time consuming, it is the *nature* and not the *amount* of experimentation that is determinative of non-enablement. *See* Hybritech v. Monoclonal Antibodies, Inc., 231 USPQ 81 (Fed. Cir. 1986).

The Examiner's rejection is also in direct odds with the Examiner's asserted obviousness rejection. In particular, the Examiner cites prior art directed to a bacterial alpha-amylase with extremely low homology to SEQ ID NO:2, yet maintains that based on this reference, an artisan would be motivated (and implicitly enabled) to make the corresponding alterations in a fungal alpha-amylase. If an artisan is enabled to make alterations from a very low homologous enzyme

in the claimed enzymes, why is an artisan not enabled to make the claimed alterations in much more structurally related enzyme?

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. The Rejection of Claims ? under 35 U.S.C. 112

Claims 42-48 are rejected as allegedly not supported by an adequate written description, as required under 35 U.S.C. 112, first paragraph. The Examiner contends that the specification does not provide written description support for amino acid sequences having 70 to 99% identity to SEQ ID NO:2. This rejection is respectfully traversed.

The written description requirement of the Patent Code is fulfilled when the patent specification describes the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See* Vas-Cath, Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The written description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *See* In re Marzocchi, 169 USPQ 367 (CCPA 1971).

Under this standard, the Examiner's conclusion that the specification only provides adequate written description support for SEQ ID NO:2 is plainly incorrect. The specification discloses, and one skilled in the art would clearly recognize, that the scope of the present invention includes polypeptides having at least 90% identity to SEQ ID NO:2. An artisan would reasonably conclude that Applicants were not only in possession of SEQ ID NO:2, but also that Applicants had possession of highly related sequences, as specified by the claims. Examples of alpha-amylases falling within the scope of the claimed invention include alpha-amylase having conservative amino acid substitutions in the amino acid sequence of SEQ ID NO:2, which are clearly envisioned by an artisan once apprised of Applicants' invention. Other examples include the alpha-amylases claimed in the parent patent US Pat. No. 7,005,288.

The Examiner has also not provided sufficient evidence or reasoning to rebut that the specification provides an adequate written description for highly homologous amylases claimed. In this regard, the Examiner contends that a number of additional representative species are required to be disclosed. However, given the high degree of identity, an extremely high degree of predictability exists as to the structure and function of alpha-amylase falling within the claims.

Therefore, Applicants respectfully submit that the specification contains a sufficient description of the structural and functional characteristics of the claimed polypeptides to fulfill the requirements of 35 U.S.C. 112. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 31-41 under 35 U.S.C. 103

Claims 31-41 are rejected under 35 U.S.C. 103 as obvious over Christenson in view of Matssura and Svendsen. Christianson is directed to bacterial protease enzyme and methods for producing same. Matsuura et al. discloses fungal alpha-amylases, but does not teach or suggest the alterations recited in the present claims. Svendsen et al. is directed to bacterial-related alpha-amylase variants. The Examiner contends that Svendsen et al. teaches that all alpha-amylase have conserved regions, and that the alterations in Svendsen et al. are equivalent to the alterations in the fungal-related alpha-amylase variants of the present invention. This rejection is respectfully traversed.

None of the cited reference teach or suggest the variant fungal-related alpha-amylases recited in the present claims. The alterations of Svendsen et al. are based on the aspects of bacterial-related alpha-amylases, i.e., Termamyl-like alpha-amylases, which have very low homology and extremely low identity to the fungal related alpha-amylases of the present invention. Although Svendsen et al. teaches that there is some conservation between the bacterial and fungal alpha-amylases, Svendsen et al. does not suggest to an artisan to make the specific claimed alterations in a fungal related enzyme. Absent a teaching that the alterations disclosed in Svendsen et al. are applicable to the fungal alpha-amylase, an artisan would not have any reasonable expectation of success since the alpha-amylases of Svendsen et al. have a very low degree of identity to the alpha-amylases claimed. The Examiner references Svendsen et al.'s teaching that there are both similar and different regions, yet the Examiner does not explain how this would lead a skilled artisan, absent a high degree of sequence identity, to reasonably expect that alterations in Svendsen et al. would be applicable to fungal related enzyme. In fact, the Examiner has not provided any evidence supporting that an artisan would have a reasonable expectation of success.

The Examiner argues that Applicants enablement arguments support the obviousness rejection. However, although the art enables an artisan to generally prepare highly homologous

alpha-amylase sequences, there is no specific guidance to make the claimed alpha-amylases with a reasonable expectation of success. As the cited alpha-amylases of Svendsen et al. have a very low homology to the claimed alterations, an artisan would not have a reasonable expectation that making corresponding alterations in a very distant alpha-amylase would be successful.

Therefore, Svendsen et al., alone or in combination with Christianson et al. and Matsuura et al., clearly does not suggest the alterations in fungal-related alpha-amylases, as claimed in the present invention.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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